Y 4. EN 2/3: 99-II

99th Congress
2d Session | COMMITTEE PRINT | COMMITTEE PRINT 99-II

COMPLETED
60
NF 213

PROCEEDINGS OF A WORKSHOP ON VACCINE INNOVATION AND SUPPLY

REPORT

PREPARED BY THE

INSTITUTE OF MEDICINE,
NATIONAL ACADEMY OF SCIENCES

FOR THE USE OF THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

ORIGINAL

AUGUST 1986

U.S. GOVERNMENT PRINTING OFFICE
62-465 O WASHINGTON : 1986

For sale by the Superintendent of Documents, Congressional Sales Office
U.S. Government Printing Office, Washington, DC 20402

CDD
I
BEST COPY AVAILABLE
62-465 O - 86 - 1

COMMITTEE ON ENERGY AND COMMERCE

JOHN D. DINGELL, Michigan, *Chairman*

JAMES H. SCHEUER, New York
HENRY A. WAXMAN, California
TIMOTHY E. WIRTH, Colorado
PHILIP R. SHARP, Indiana
JAMES J. FLORIO, New Jersey
EDWARD J. MARKEY, Massachusetts
THOMAS A. LUKEN, Ohio
DOUG WALGREN, Pennsylvania
BARBARA A. MIKULSKI, Maryland
AL SWIFT, Washington
MICKEY LELAND, Texas
RICHARD C. SHELBY, Alabama
CARDISS COLLINS, Illinois
MIKE SYNAR, Oklahoma
W.J. "BILLY" TAUZIN, Louisiana
RON WYDEN, Oregon
RALPH M. HALL, Texas
DENNIS E. ECKART, Ohio
WAYNE DOWDY, Mississippi
BILL RICHARDSON, New Mexico
JIM SLATTERY, Kansas
GERRY SIKORSKI, Minnesota
JOHN BRYANT, Texas
JIM BATES, California

NORMAN F. LENT, New York
EDWARD R. MADIGAN, Illinois
CARLOS J. MOORHEAD, California
MATTHEW J. RINALDO, New Jersey
WILLIAM E. DANNEMEYER, California
BOB WHITTAKER, Kansas
THOMAS J. TAUKE, Iowa
DON RITTER, Pennsylvania
DAN COATS, Indiana
THOMAS J. BLILEY, Jr., Virginia
JACK FIELDS, Texas
MICHAEL G. OXLEY, Ohio
HOWARD C. NIELSON, Utah
MICHAEL BILIRAKIS, Florida
DAN SCHAEFER, Colorado
FRED J. ECKERT, New York
TRENT LOTT, Mississippi

WM. MICHAEL KITZMILLER, *Staff Director*
THOMAS M. RYAN, *Chief Counsel*
ANTHONY ROBBINS, *Medical Consultant*
LINDA G. STUNTZ, *Minority Counsel*

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

JOHN D. DINGELL, Michigan, *Chairman*

RON WYDEN, Oregon
DENNIS E. ECKART, Ohio
JIM SLATTERY, Kansas
GERRY SIKORSKI, Minnesota
JAMES H. SCHEUER, New York
JAMES J. FLORIO, New Jersey
THOMAS A. LUKEN, Ohio
JOHN BRYANT, Texas
HENRY A. WAXMAN, California
RICHARD C. SHELBY, Alabama

NORMAN F. LENT, New York
THOMAS J. BLILEY, Jr., Virginia
MICHAEL G. OXLEY, Ohio
MICHAEL BILIRAKIS, Florida
DAN SCHAEFER, Colorado
FRED J. ECKERT, New York
TRENT LOTT, Mississippi

MICHAEL F. BARRETT, *Chief Counsel/Staff Director*

NINETY-NINTH CONGRESS

JOHN D. DINGELL, MICHIGAN, CHAIRMAN

ROOM 2323
RAYBURN HOUSE OFFICE BUILDING
PHONE: (202) 225-4441

U.S. House of Representatives

Subcommittee on Oversight and Investigations
of the
Committee on Energy and Commerce
Washington, DC 20515

July 28, 1986

LETTER OF TRANSMITTAL

To Members of the Subcommittee on Oversight and Investigations:

It is a pleasure to transmit this report to the Subcommittee. In response to a request from the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce and the Senate Committee on Labor and Human Resources, the Institute of Medicine of the National Academy of Sciences assembled some of the Nation's leading experts on vaccine and immunization matters. The charge to the group was very different from other recent meetings on vaccine issues because it asked the participants to put aside injury, liability, and compensation issues and to discuss other impediments to optimal use of vaccine and immunization technology. The report of the conference is contained herein.

The results of the Institute of Medicine meeting confirm what we first learned during the Subcommittee's March 1985 hearing on biotechnology and vaccines (Committee Print 99-1) -- that new technologies make new and safer vaccines possible, but these vaccines are not yet benefiting the public. This report discusses the obstacles to full vaccine use in the prevention of human infectious diseases. It also suggests possible courses of action.

The most important lesson of the conference is that industry, academia, state and local governments, and Federal agencies can create the constructive, collaborative and coordinated efforts that will assure optimal use of the most cost-effective form of disease prevention: immunization. The report will be helpful in future legislative deliberations of the Committee.

Special thanks is due to Drs. Samuel O. Thier and Roy Widdus and Subcommittee Counsel Phyllis Freeman for the rapid response from the Institute.

Sincerely,

JOHN D. DINGELL
CHAIRMAN

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

SAMUEL O. THIER
PRESIDENT

June 19, 1986

The Honorable John D. Dingell
Chairman
House Committee on Energy and Commerce
Rayburn House Office Building, Room 2125
Washington, D. C. 20515

Dear Chairman Dingell:

In response to your letter of March 6, 1986 the Institute convened a group of experts from academe, government, and industry to discuss the vaccine policy issues which you raised. The workshop which was held April 24-25 was supported by the Carnegie Corporation of New York and by independent funds of the National Research Council. No formal recommendations were requested of the participants or of the Institute of Medicine and none were made. However, a series of very important concerns was identified and discussed. There was a clear sense that the new age of vaccines provides unprecendented opportunities. The liability issue is not the only policy area which must be addressed to make optimal use of this enormously cost-beneficial technology for disease prevention.

The approach suggested in your letter, of putting vaccine injury, liability, and compensation aside for this workshop, was most effective. While all participants retained their awareness of the central importance of the liability issue, they were able to focus on the additional series of critical questions that must be addressed. This workshop emphasized that solving the liability problem alone will not result in the full use of new and improved vaccines.

The experts at the workshop agreed that progress in vaccine technology makes it possible to prevent infectious diseases to an extent unimagined only a few years ago. As you know, there is no real debate about the cost effectiveness of vaccine disease prevention as compared to most treatment strategies. It is on the strength of these basic facts that the Congress may want to act to enhance optimal use of the new technology.

The Institute of Medicine would be pleased to be of any further assistance to you.

Sincerely,

Samuel O. Thier, M.D.

cc: Senator Orrin Hatch

IV

BEST COPY AVAILABLE

TABLE OF CONTENTS

	PAGE
Introduction	1
Research	3
Development	6
Clinical Trials	8
Licensing and Quality Control	9
Production and Procurement	11
Distribution and Use	14
Surveillance and Monitoring	16
Conclusion	18

Appendices

1. Letter from Chairmen Dingell and Hatch to Dr. Thier
2. Invitation Letter to Participants from Dr. Thier
3. Workshop Agenda
4. Opening Remarks of Dr. Thier
5. Introduction to the Problem: A Congressional Perspective, Dr. A. Robbins
6. List of Chairmen of Working Groups, Membership of Groups, and Designation of Notetakers
7. Alphabetical Attendance List of Participants with Professional Affiliation and Address
8. Charges to Each of the Seven Working Groups
9. Special Areas of Concern to the Research Working Group
10. Letter of Thanks from Senator Hatch to Dr. Thier

BEST COPY AVAILABLE

NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVENUE
WASHINGTON, D. C. 20418

INSTITUTE OF MEDICINE

MEMORANDUM

TO: Samuel Thier

FROM: Phyllis Freeman, Scholar-in-Residence

DATE: June 18, 1986

SUBJECT: April 24-25 Vaccine Workshop

Attached is the summary of the April 24-25 meeting on those vaccine policy issues for which Chairmen Dingell and Hatch requested you convene a workshop. What I believe may be of great use to the Congress is the clear sense of the group of experts from academia, government, and industry that the new age of vaccines provides unprecedented opportunities; and that the liability issue is not the only policy area which must be addressed to make optimal use of this enormously cost-beneficial technology for disease prevention. This perspective was posed as a question at the start of the meeting and presented as a conclusion by the close.

Because no recommendations were requested of the participants or of the Institute, and no strict outline was followed within sessions, the discussions ranged over a wide set of topics without any uniformity of structure. As a result the proceedings covered a great deal of important material but do not fit into a tight, analytic framework. I suggest the proceedings be read for the inventory of problems that were defined, the range of solutions which were contemplated, and the nature of the debates that will emerge.

The solutions considered anticipate government sponsored incentives for the industry and academia, and their contributions to public health goals. More coordination among activities of government and nongovernmental organizations was favored. Often reiterated was the point that the different aspects of vaccine and immunization efforts are complementary but that participants in one phase are not particularly aware of the requirements of another stage in the process. Similarly, even some of those who were most aware of domestic production experience were surprised to learn the procurement history and future needs of the United Nations immunization programs of which the U.S. has been very supportive. That is, the demand is increasing dramatically and the prices on the international market are a tiny fraction of those in the United States.

BEST COPY AVAILABLE

Although there was considerable controversy over the form and forum for coordination of vaccine and immunization efforts, there was widespread discussion of the need for some additional mechanism for cohesion which is consistent with the earlier work of the IOM in the report of Vaccine Supply and Innovation. Participants expressed their appreciation for the contributions of the agencies which have borne major responsibility for implementing the vaccine and immunization programs thus far, while stressing the exponential nature of the workload and the opportunities the biological revolution offers.

Even though the working groups ran simultaneously I attended some portions of each in order to familiarize myself with the participants and the tone of the discussions. To prepare the summary I reviewed the notes taken by a designated person within the group, listened to the entire tape of the plenary session, and reviewed those portions of the working group tapes which contained particularly interesting or controversial material. I also relied on the working group tapes to clarify and supplement statements made in the plenary and to fill in where the notes did not provide an adequate basis for my understanding. As you will see in the Table of Contents, the proceedings are followed by a series of appendices.

I believe the assembled experts have provided a good basis for the lawmakers to augment their understanding of the issues and the arguments as to how to proceed to reap full value of the new science while promoting life and conserving health dollars.

BEST COPY AVAILABLE

Introduction

The April 1986 workshop on vaccine issues represents a continuation of the Institute of Medicine's (IOM) major studies (1) New Vaccine Development: Establishing Priorities, Volumes I and II (1985; 1986), and (2) Vaccine Supply and Innovation (1985). The Institute sponsored the event on April 24 and 25 in response to a letter request from Chairmen Dingell and Hatch (see Appendix 1). The request was based on the perception that:

> . . . the revolution in biotechnology makes it possible to contemplate new and improved vaccines that would become available very quickly if research, development, and production were to go forward rapidly. However, we also know that this is not happening: competition for limited research funds and reluctance on the part of the vaccine makers to invest in new vaccines retard these advances.
>
> There is now great interest in both Houses of Congress in legislation that would remove one impediment to new vaccine development -- concern over liability for injury caused by vaccines. This legislation may be enacted, and this would help protect the current vaccine supply. We are writing, however, because we believe that the United States needs an organized program to assure full benefit from new and improved vaccines. New vaccines and vaccines requiring improvement identified in the Institute's first report must be encouraged through research, development, clinical trials, licensing, and production into full use.

At the invitation of Dr. Samuel O. Thier, President of the Institute of Medicine (see Appendix 2), some 70 vaccine and immunization specialists from academia, government, and industry assembled. They were greeted and charged by Dr. Thier (see Appendix 4). He emphasized that both the prior IOM vaccine activities and this workshop

> . . . have attempted to develop ideas which would complement rather than replace the system which exists in this country for vaccine research, development, production, supply, and use. There are both strengths and gaps in that system but the challenge to you today is to make suggestions to identify ways to strengthen further what we have and make its parts fit into a more cohesive whole--a system the nation can understand and rely upon. We want to take full advantage of the new techniques now available for making vaccines, so there will surely be some new elements to add to our national capacity in the coming years.

Next Dr. Anthony Robbins, Professional Staff, House Committee on Energy and Commerce presented the issues of concern to Chairman Dingell on behalf of his Oversight and Investigations Subcommittee. He explained that the Congress has been aware of the important issues of injury, liability, and compensation and will, most likely, address them soon. In contrast, "Throughout the continuing debate on these

BEST COPY AVAILABLE

issues, no one has suggested that a remedy to these acute legal problems will create an adequate and reliable program to prevent disease using new and improved vaccines." He asked, "Can you help the Congress understand the issues and design the future program for research, development, and use of vaccines and immunization to prevent human disease?"

Dr. Robbins also made the point that the timing of the Congressional request is tied not only to the pressing questions about liability, but also to the Congress' support of the urgent program of the United Nations to immunize children around the world (see Appendix 5 for full text):

> It is probably useful to understand why the Congress requested this workshop now. I believe there is a very real opportunity to apply the collective experiences to Congressional deliberations if they can be captured today. Congress is already focused on vaccines: the injury issue, the threat to the current supply, and the work of the international campaign to immunize all children by the year 1990. If the Congress chooses to legislate on these issues, why not do the job correctly and create a program to assure effective research, development, production, and use of vaccines?

All participants were pre-assigned to one of seven working groups (see Appendix 3 for Agenda) which covered all phases of the vaccine and immunization process: Research; Development; Clinical Trials; Licensure and Quality Control; Production and Procurement; Distribution and Use; and Monitoring and Surveillance. Each group had an assigned chairman (see Appendix 6 for chairmen and participants in all working sessions; Appendix 7 for alphabetical participant address list) and informal charges (see Appendix 8) to guide the discussions. Institute staff and some participants assisted the chairmen in each working group by taking notes (see Appendix 6). Congressional staff and other interested parties observed the conference including the working sessions.

All chairmen met in the evening to discuss the day's deliberations with Drs. Robbins and Helms from the requesting Congressional Committee staffs and IOM staff and to plan the plenary session, to be chaired by Dr. D.A. Henderson, Dean of Johns Hopkins School of Hygiene and Public Health. In the following morning's plenary session each of the seven chairmen summarized the work of his group and all participants were encouraged to comment or raise questions.

In closing, Dr. Charles Helms, staff to Senate Committee on Labor and Human Resources, offered some comments on behalf of Senator Hatch. He thanked the IOM and all of the participants for laboring on this complex set of important questions and for providing some answers. He echoed his perception that the questions addressed merit the thoughtful attention they are beginning to receive. He concurred that the liability problem is not the only policy issue of major importance in vaccine innovation and supply. (See Appendix 10 for letter of thanks from Senator Hatch to Dr. Thier.)

A review of the workshop discussions and plenary session presentations follows.

BEST COPY AVAILABLE

The research discussions underscored optimism about the potential of the new science to provide a "tidal wave" of new vaccines; however, some frustration and skepticism was expressed about the readiness of the rest of the system to develop, produce and distribute the full range of known vaccine candidates and those which will be created in the coming years.

This group discussed their shared scientific vision of a coming era when we will be able to make vaccines against an enormously expanded range of pathogens. This optimism grows out of the new theories and techniques of molecular biology as well as other advances in basic science. The profusion of new "candidates" for development reflect these remarkable gains. Over the first two hundred years of vaccine work approximately 20 were created and only a handful of those are regularly in widespread use. In recent years many more have been conceived. During this IOM conference the Department of Defense (DOD) heralded 42 new candidates for development; National Institute of Allergy and Infectious Diseases (NIAID) 28; and Rockefeller Foundation 6.

The research scientists summarized the areas of basic science which must be expanded if the biological revolution is to yield prevention against the full range of infectious diseases. The applied research needs have been presented in a more comprehensive and scholarly fashion elsewhere (including in IOM's New Vaccine Development: Establishing Priorities, Volume 1. Diseases of Importance in the United States). In the workshop two short summaries were presented.

1. A National Institutes of Health (NIH) basic scientist listed three areas where there will be a continuing need for more fundamental knowledge to develop new approaches:

   - o about the organisms (pathogens)
   - o about how the organisms cause disease (pathogenesis)
   - o about how the organism relates to the host and the host immune response (immunologic defenses).

2. The research group chairman indicated that there are true research issues (as opposed to applied or development efforts, that are directly tied to vaccines). He listed the following as keys to basic science:

   - o anti-idiotypes as vaccines (these are anti-antibodies that mimic the surface structure of the original pathogen antigen against which the first antibody was induced)
   - o antigenic variation and ways to combat it
   - o molecular basis of attenuating virulence
   - o vectors (the potential of vector vaccines, e.g., vaccinia)
   - o mucosal vaccines (the role of secretory antibodies)
   - o carbohydrate vaccines (immune response to carbohydrate antigens)
   - o age group specific vaccines (immune mechanisms in the very old and very young)

BEST COPY AVAILABLE

It was observed that all but one of the scientists discussing research gains and needs had backgrounds in virology. The absence of more parasitologists was attributed to lack of corporate interest in vaccines against parasitic diseases. One participant from industry suggested that the financial incentive does not exist when the disease is not present in the U.S. population.

The Development work group called for more research to create model systems to predict vaccine efficacy while reducing the need for animal studies. This would relieve some of the conflict with animal rights activists. To reduce risk of injury to humans in large scale clinical trials they suggested improvements in animal models which would allow earlier prediction of efficacy. In those cases where efficacy does not appear to be adequate, further trials to evaluate safety would be obviated. The Development group saw this as a task for the researchers.

Because the prospect for accelerating vaccine development was apparent to basic scientists at NIAID by the late 1970s, "priority analysis" is well developed. The NIAID staff first identified priorities among vaccine candidates in a three day conference in 1981. A sophisticated methodology for generating vaccine development priorities was completed by IOM for NIAID in 1984. During the session a NIAID participant indicated that periodic review and updating of these priorities would be useful in setting priorities for later stages of vaccine preparation and use, and could be done by NIAID. It was also agreed that the method used by IOM to derive the lists for New Vaccine Development: Establishing Priorities, Volume 1. Diseases of Importance in the United States and Volume 2. Diseases of Importance to Developing Countries is available and the computer program is ready to be rerun.

Because scientific breakthroughs and changes in disease incidence and morbidity will occur, it will be important to adjust the development priorities over time. No specific recommendation was made as to how often overall priorities should be thoroughly reviewed but suggestions of two to three years were mentioned.

There were two short, but interesting debates about the impact of biotechnology. The participants pointed to research needs and questions to be addressed when evaluating a vaccine for licensure. One example is the fidelity with which expression systems such as yeast synthesize foreign proteins, i.e., are they glycosylated and uniformly the same length as the protein? This raises questions of the criteria for licensure review. Should criteria for products made with the techniques of biotechnology be different from those used for traditional vaccines? It was suggested by some participants that the existing criteria should not be changed as the new techniques are more precise. However, others questioned how accurately scientists can predict the consequences of the genetic interventions including transfers of genetic information to other species. The question was not resolved.

A related debate had to do with whether recombinant vaccines will have fewer side effects than traditional products. Participants agreed that the greater purity of the new products is good, but purity is not the only factor to consider when analyzing potential side effects. More knowledge must be generated before scientists will be able to determine fully the safety of the new products.

BEST COPY AVAILABLE

The discussion focused on the continuing inadequacy of governmental and industrial investment in this extraordinarily cost beneficial area of preventive health despite a strong record of priority setting based on the cost effectiveness of immunization. The participants were not sanguine that their work would be carried through to its public health application. Among basic researchers the most frequently expressed concerns about high priority vaccines were these:

1. Clinical trials are stalled for lack of money from government and industry.

On the government side the shortfall was attributed to critical shortage of contract monies as grant funds are cut back and NIH struggles to stabilize the support of basic research. Reprogramming of research funds for AIDS was also cited as a detracting factor from other high priority projects. A list prepared at NIH includes among the ready but unfunded vaccine trials: hepatitis B, group B streptococcus, and hepatitis A. An industrial participant asked how more university researchers could be enticed into clinical evaluation of new vaccines like herpes, which have been prepared, but literally shelved in the freezer for lack of attention to next steps. A hepatitis B vaccine candidate was similarly described.

2. Valuable developmental projects stymied for lack of funds. Among the most important projects which are ready at NIAID but not underway are:

   - o Enhancement/Potentiation of Vaccine Antigens
   - o Procurement of Purified Viral Antigens (respiratory syncytial virus, parainfluenza viruses types 1 and 3, influenza viruses A and B)
   - o Development of In Vitro Assays for Assessing Toxicity and Potency of New Pertussis Vaccines and/or More Appropriate Animal Models
   - o Alternative Study Sites for Performance of Efficacy Trials with New Acellular Pertussis Vaccine(s)
   - o Development of Newer S. pneumoniae Vaccine Antigens
   - o Phase 1 Trials of a Candidate Gonococcal Vaccine

3. There are no known sources to pay for vaccine for developing countries when the disease does not also exist in industrial nations. AN NIAID participant said research on these vaccines continues although complete development is unlikely. (The DOD works on many of these same diseases to protect military personnel.)

4. The increasing number of applications to the Food and Drug Administration (FDA) will stress severely the capacity of that agency, especially in light of the novelty of some of the new manufacturing processes. (Even though the number of vaccine candidates for licensure is far short of the potential of the science, it is still a greater burden to the regulators than in previous years, especially in light of the need to evaluate the new manufacturing techniques involving biotechnology.)

BEST COPY AVAILABLE

5. The small number of U.S. commercial producers was seen to be a very significant problem.

6. Frailties in the vaccine distribution mechanism in the U.S. and world-wide were cited with concern.

7. Lack of awareness by the citizenry of the enormous practical value of these scientific achievements.

All of these concerns were addressed in other sessions. The research group closed by noting a demoralization of the researchers where their work is stalled or not used. This group identified three special areas of concern: funding, the need for an advisory/advocacy group, and criteria for licensure (see Appendix 9).

The Production and Procurement group raised two issues relevant to vaccine research. A UNICEF participant pointed out that if it were not for short shelf life and need for the "cold chain" (refigeration from point of manufacture on to keep vaccines from spoiling before reaching children in the field), the international immunization programs could be delivered far less expensively. Work on heat stability has always been a high priority for developing countries.

Development

The work groups on development, clinical trials, and licensure and quality control had overlapping mandates because development was defined broadly: to begin where researchers have identified an attractive candidate immunogen and range across all activities including clinical studies and licensure until a new or improved vaccine is approved for marketing.

The development session described two ways to define their area: (1) the time period as set out above; and (2) the elements involved in going from small to large scale production capability.

The following elements are included in the development phase: scale up and yield, use of appropriate facilities and equipment, toxicology, serology, a decision to go forward into eventual production influenced by marketing analysis, production of consistency lots, preparation for manufacture, clinical studies, and regulatory evaluations and decisions.

It was noted with special emphasis that development is the phase of vaccine/immunization work where a decision is made to go forward--or not--to produce a new product. It was a participant in the Production and Procurement session who noted a fundamental difficulty for new vaccines: there are very few firms interested in doing development from preclinical phase into field trials. This statement is based on a recent survey conducted by the DOD. An industry participant responded by saying that despite the survey results, more firms might be willing to do development work if they understood the specific public health need, the future use, and the specific requirements of the vaccine for efficacy and safety. This led the Production and Procurement group to discuss the possibility of the Advisory Committee on Immunization Practices (ACIP) of the Public Health Service moving up the time of its recommendation to precede clinical trials. An earlier recommendation would encourage industry R&D. The ACIP would

BEST COPY AVAILABLE

have to define specifications of an acceptable vaccine. It would then express its recommendation as contingent on a candidate meeting those criteria.

An industry participant (in Production and Procurement) went on to suggest that perhaps the government should conduct or support development work and then contract with firms for production. This approach is most attractive in the case of vaccine candidates where industry sees insufficient market incentive to invest independently. Success would depend on government knowledge of industrial planning for each high priority vaccine candidate. Currently the Public Health Service (PHS) and academics have no regular access to information about industrial planning. Nor is there a concerted PHS effort to assure development. Only the Army has an office with responsibility to plan development strategies for each of its vaccine candidates. The civilian side has no such office nor funds to support lagging development efforts.

The Development work group focused on deficiencies and on needed improvements: (1) epidemiological centers; (2) skilled personnel for industry; and (3) financial incentives to industry.

Surveillance of disease incidence could improve decision making on medical needs and market opportunities early in the development process. The Development group expressed a need for a few, large scale, epidemiological centers to do long-term work with representative populations. They also noted that these same centers could provide important data for the surveillance and monitoring of the impact of immunization programs. In addition to looking at infectious disease attack rates, these centers could also study rates of primary medical incidence of convulsions, sudden infant death, and other critical baseline data. This could improve discrimination between the rates of nonvaccine and vaccine-related incidents.

The same facilities could also be used for clinical trials studying both antibody responses and side effects and for post-market surveillance. A great deal of emphasis was placed on the last activity.

It was reported by some that the industry has an inadequate supply of genetic and process engineers to scale up from test batches to full production. An industry participant said the firms compete heavily for the few, skilled personnel in these fields, more often hiring experienced hands away from another company rather than from new sources. The group's chairman believes that centers of excellence for training should be designated and assisted, perhaps by the National Science Foundation, to overcome this shortage. The cause was described by an industry participant to be the shrinkage in the industry from 14 major U.S. firms in earlier days to only 4 remaining. Programs like those at Purdue and Lehigh Universities could be encouraged to expand to meet the bioengineering needs.

Financial incentives for the industry were seen as essential if firms are to help develop vaccines for populations in developing countries; for military personnel who may become exposed to diseases not present in the U.S.; and for those at risk for diseases which afflict only small groups within the U.S. These vaccines might be called "orphan products." The incentives to overcome current lack of industrial enthusiasm in these three areas include:

- o more rapid depreciation of bricks and mortar
- o long term contracts

BEST COPY AVAILABLE

- o longer patent protection
- o programs offering market exclusivity, such as "buy America"
- o grants for facilities.

This group also identified a need for standard reagents, standard tests, and materiel to expedite the development process. Both the DOD and the NIH have demonstrated interest in specialized sites for manufacture. As a joint project NIH and DOD are currently exploring creation of a plant to make test batches of vaccines. Even with 42 vaccine candidates and a $40 million budget the military is stymied and unable to proceed with important field trials for lack of a sufficient quantity of vaccine. This shortage is particularly acute where total sales or use for a given vaccine is anticipated to be small.

It is important to note several overriding concerns which came out of the development discussions. To achieve appropriate public health benefits from vaccines, government health officials need to buy targeted research. For example, there is a need for development of methods for producing particular proteins in mammalian "expression systems." There is also a need for development of methods for producing antigens on a commercial scale ("scale-up"). They also need better knowledge about which vaccines the industry is developing and which it is neglecting.

The group agreed there must be development of vaccines for international use, even for diseases not encountered in the U.S. The chairman summarized by saying that the interest in the U.S. for these vaccines has been so low as to be virtually out of sight. Now that the need has been recognized, the record should be improved; government financial assistance to the industry is needed if U.S. firms are to contribute to this aspect of the global effort. The only alternatives are for the government to do the work directly or for the United States not to provide any significant support.

Clinical Trials

The Clinical Trials group worked from the shared premise that there are a series of deficiencies which, if unremedied, will delay use of new and improved vaccines. The group expressed confidence in the efforts of NIH, the Centers for Disease Control (CDC), and FDA and simultaneously urged the formation of a strong advocacy group to review all aspects of vaccine and immunization programs to overcome the current and anticipated barriers.

Clinical trials are known by industry to be the most expensive step in development. Even participants from established firms questioned how they can know what FDA will ultimately find to be an acceptable clinical trial. The group called for more consultation from FDA, NIH, and CDC to provide more certainty about all aspects of study design from conception through analysis.

Session participants also urged standardization of tests to gauge adequacy of response to a vaccine. They report that much of this work has been done and that standardization is possible. The body of knowledge must be readily available to facilitate this aspect of development.

BEST COPY AVAILABLE

Field tests of new or improved vaccines are sometimes most appropriately carried out with populations residing outside the U.S. This occurs where the U.S. population has already been immunized against the disease or where it is not endemic in this country.

International organization participants concurred that ethical issues can be analyzed and satisfactory criteria spelled out. Important issues include:

- o legitimate participation by investigators in the host countries
- o educational spin off to the host country so that knowledge about vaccine research and production is increased
- o testing only where the disease is relevant to the population involved
- o standards of conduct and data from tests be as stringent as if the study were done in the U.S.

Application of public health priority thinking at this stage was considered to be very important, particularly in light of the costs of clinical testing. Priorities should take into account the availability of scholars and populations for studies as well as funding limitations. Priority setting has never been coordinated for decision making on which trials to pursue. The group commented that if there were more coordination and collaboration, some qualitatively better studies might emerge, particularly for "orphan vaccines." Also, duplicative efforts could be avoided, thereby conserving precious resources to test additional vaccines.

As did the Development section, this group focused on the need for the government to identify and stimulate more activity for "orphan vaccines." Examples included vaccines for the immunocompromised, for newborns, for pregnant women, and for less common diseases like Rocky Mountain Spotted Fever.

Finally, the group made special reference to an aspect of vaccine liability which has not been addressed in any of the bills before Congress at the time of this meeting. Liability for participants in clinical trials may threaten development of new and improved vaccines; and it affects universities as well as manufacturers.

Licensing and Quality Control

Licensure continues to be viewed as a unique stage because of the need for independence in regulatory decisions. Both the Development and Clinical Trials groups raised two of the issues discussed in the Licensure session: more, early consultation on new products and standardization of criteria for efficacy by the FDA (sometimes in conjunction with NIH or CDC as appropriate).

The Licensure group itself considered five major topics after determining that no major overhaul of the laws governing licensure of vaccines is necessary, as the licensing process is working reasonably well. Needed improvements in the regulatory process were identified as follows: (1) the Investigational New Drug (IND) process; (2) prior testing in other countries; (3) periodic review to weed out obsolete or redundant requirements; (4) more uniform efficacy criteria, but consistent with margins of efficacy that may vary tremendously from vaccine to vaccine (e.g., 10 percent in one case, virtually 100 percent

62-465 0 - 86 - 2

BEST COPY AVAILABLE

in another); and (5) an examination of safety criteria, especially on the long-term effects of vaccines, which companies find difficult to meet under current FDA requirements. Items (1) and (2) are discussed below.

The Licensure group encouraged further expansion of pre-IND application discussions between FDA and companies, especially with small companies that may not be familiar with the approval process. There were concerns that many biotechnology companies will opt out of the vaccine market because of difficulties in meeting the licensing requirements. There was support expressed for pre-IND review of the testing protocols, which, if met, should lead to approval by FDA of the New Drug Approval (NDA). Apparently, there are still problems with companies believing they have done everything according to the pre-IND review, and still being required by FDA to provide additional information. (If a legislative approach to this issue is sought, there is precedence in the Medical Device Amendments of 1976, where companies may negotiate with FDA on a Product Development Protocol, which, if met, would lead to approval of the device.) The industry and FDA would benefit from more FDA technical staff, especially in the pre-IND and IND process. As an example of needed technical competence, the Office of Biologics has no in-house expertise in parasitology.

The Development group also expressed a need for additional assistance to firms, especially as new genetically engineered vaccines are prepared. They called for more anticipatory guidelines and more anticipatory consultation on the adequacy of facilities.

The availability of such anticipatory processes was considered to be critical in light of the huge investments being made by industry. The risk of waiting to readjust at the time of a licensure site visit poses an unacceptable financial risk to industry.

It was suggested that peer review groups, independent of the FDA, should be allowed to devise new safety tests and efficacy evaluation systems suitable for judging the vaccines that arise from the new technologies. The current organization has no such flexibility.

The Development group called for more workshops between NIH, FDA, and industry to continue improving communication. They also stressed a major concern that deficient FDA staffing levels may become the greatest impediment in getting the vaccines of today into use tomorrow. Specific areas that might benefit from more FDA staffing include quality control processes, protocols and tests--particularly as the industry uses novel processes.

On prior testing in other countries, the Licensure group considered two possibilities: (1) licensing a vaccine when it is licensed in other specified countries (e.g., Britain), and (2) accepting data used to gain a license in those other specified countries. Currently, FDA does accept data collected in a limited number of countries, and the discussion was focused on how to expand this use. There was no support for automatically licensing a vaccine if it were licensed elsewhere because of the need to examine the data on which the licensing decision was based.

Should broad public health priorities be imposed on FDA's review process? A vaccine policy body guiding FDA, elicited resistance from the FDA participant, fearing a direct role in FDA operations. For example, directing FDA on which vaccines should be given priority in the licensing process was seen as compromising FDA work on other vaccines and disrupting internal decision making. However, others

pointed out that FDA has a priority system for drugs, which could be applied to vaccines. The purpose would be to maximize public health benefits. Thus, the question seemed to be whether a priority system would be imposed on FDA or adopted by it.

On the role of FDA in contributing to a national vaccine policy, it was the strong opinion of the group that FDA should not be involved in promoting any particular vaccine or even be involved in activities that might give the impression that FDA was promoting specific vaccines.

Production and Procurement

This area dealt with three major topics: vaccine supplies for U.S. civilian use; those for military personnel; and vaccines for international programs serving the developing nations. Unlike any other work group, this one began with consideration of international needs and markets. It examined the unique role of the military as a bridge between international immunization programs and domestic ones, particularly in the area of new vaccines, and it analyzed the U.S. situation in the global context.

A UN participant reported on the vast increase in demand for vaccine for the Expanded Program on Immunization (EPI). In 1985 UNICEF purchased 450 million doses of vaccines for the EPI (UNICEF manages consolidated purchases for many countries excluding China, Latin America and industrial nations). This represents an increase of approximately 300 percent since 1982. UNICEF projects a need for one billion doses of the same six vaccines (DTP, measles, polio, BCG) by 1990--an additional 220 percent increase over 1985.

The total price for the 450 million doses for 1985 was only $14 million. This is for 10-20 dose vials with prices based on low bids of:

10¢/dose	measles
2¢/dose	DTP
1¢/dose	tetanus
3¢/dose	oral polio
7¢/dose	BCG

Vaccine expenditures now represent only 10 percent of the cost of this immunization program. Other major expenses associated with the cold chain and short shelf life could be reduced by finding better methods of stabilization.

No U.S. manufacturer currently participates in bidding for contracts through UNICEF (or the Pan American Health Organization's [PAHO] revolving fund for Latin America). As a matter of policy UNICEF has chosen not to rely on a single supplier for any of its vaccines. Not all U.S. industrial participants were even aware of these international prices which are lower than U.S prices by a factor of 10 to 100. (In the case of DTP it is a factor of almost 10 to 400.) Several observers noted that their companies could not afford to fill vials with saline for the UN prices.

Connaught (Canada), the one North American company present which does supply UN contracts explained that at the current level of demand the companies were selling excess capacity at marginal cost. Orders

BEST COPY AVAILABLE

to supply 1 billion doses for 1990 would exceed excess capacity and require companies to expand their facilities. As a result, the prices for existing vaccines are not stable, even where the original R&D investment has long since been recaptured.

Prices of new vaccines where R&D costs are included are expected to be considerably higher than those for existing vaccines. No formula for predicting the costs of new products was discussed. An additional complexity has to do with the virtual absence of a U.S. or other industrial country market for many of the highest priority vaccines for international use. Aside from military personnel and U.S. travelers to the developing countries there is no domestic need. Malaria was cited as an example. A British industry participant suggested that the World Bank might be a source of payment for such an essential product.

Because the military is interested in many of the same diseases that debilitate third world populations, their research, development, production and procurement activities are seen as a potential connector between U.S. and global immunization programs. The Army has sought manufacturers to advance its 42 candidate vaccines through the final stages of development and into production. Its recent contract study on U.S. industrial capacity, Biological Scale-up and Production Resources, indicates that while there appears to be a sufficiency of companies claiming capability, there is surely an insufficiency of those willing to make contracts with the military at this time. (The study had no mechanism to test the reliability of any potential manufacturer's self description of capability.)

An Army participant noted that the DOD expresses the desire to procure vaccines at the lowest price available, but is, in fact, very inclined to support the U.S. industrial production base even where a foreign manufacturer might offer a lower price.

Given the indications of limited industrial interest in military vaccine contracts, the Army has explored gearing up for production itself. Because there are disadvantages in operation of an Army facility, including staffing and the wide range of products needed, government production is not viewed as the preferred model. The Army hopes to achieve greater cost effectiveness by contracting with commercial firms possessing production capacity and flexibility for technical staffing.

Concern for the U.S. civilian population centered on questions of consistency of supply and prices for existing vaccines as well as new and improved ones.

The entire U.S. vaccine market was said to be $330 million a year with industrial investments in R&D of $40 million. The group's chairman noted, in the plenary session, that sales of all vaccines amounts to no more than one half the U.S. market for antacid.

Manufacturers said they want greater profit margins for vaccines than they have now at U.S. prices. The whole field of vaccines can be appropriately described as one of "orphans" when contrasted with pharmaceuticals.

A very important observation about public policy guided the group to distinguish between vaccines and drugs on a more positive basis. The vaccine market is as predictable as it is limited. That is, policy makers can predict the number of doses needed of each vaccine each year to achieve public health priorities. Such certainty and conservation of health dollars is not achievable with drugs used

BEST COPY AVAILABLE

repetitively for treatment of an unknown number of cases of any infectious disease.

Public health policy makers and producers can know the total requirements and therefore, the total market well in advance, for many vaccines. If the anticipated doses are not used, it is evidence of flaws in the delivery system and subject to public health intervention. Vaccine distribution mechanisms have long been a subject of public policy at all levels of government, especially for children at school entry state laws. Failures in distribution and use now exist for Hemophilus influenzae type b (early use), and S. pneumoniae and hepatitis B (adult use).

Unlike UNICEF, the U.S. is currently relying on single producers for its supply of major vaccines. The group did not express distress at this circumstance, so long as adequate stock piles are maintained to avert interruptions in immunization schedules should there be a break in supply. Current stockpiles are not sufficient and the recent incident with DTP was cited as an example. (In 1984 there were bad lots of vaccine due to flaws in the diphtheria component.)

The states which produced their own DTP (Massachusetts and Michigan) suffered no disruption in their immunization programs when some lots of Lederle's DTP did not meet the manufacturer's requirements for release. Other states were forced to extend the time between doses beyond the recommendations of the ACIP and professional associations such as the American Academy of Pediatrics and the American Academy of Physicians. But the state lab participants did not urge the proliferation of state vaccine production facilities in response to the supply dilemma. One said that vaccine production is so difficult that new starts would be slow and costly in states where no experience and tradition exists. The other questioned whether enough trained technical people could be found to staff additional facilities (see discussions on vaccine development and production staff in the Development section, p. 7). One advantage of the small state facilities is that they are capable of making "specialty" vaccines where the market is too small to attract industrial investment. Cytomegalovirus immune globulin for transplant patients was mentioned as one such project of the Massachusetts state vaccine facility.

Vaccine prices are rising at a faster rate than the government budgets which pay for approximately one half of the vaccines used in the U.S. In response the government will buy a smaller quantity, thereby harming the immunization programs and fueling increases in health care costs to treat infectious disease patients (see section on Distribution and Use). The only optimistic comment on future vaccine prices was made by producers. If the liability issue is resolved, they expect to see increased competition. There are both U.S. and foreign firms which are not currently providers to our immunization programs that are contemplating vaccine production and U.S. sales. Presumably, competition might hold down prices where a sole producer has no such incentive.

Supplies and prices of new and improved vaccines for use in the U.S. were discussed. Given the consensus on the cost effectiveness, the policy alternative discussion focused on ways to encourage production of high priority products.

As discussed in the section on Development, there was some industrial support for the direction NIH and the Army are already taking. They are establishing a development facility to work on prevention of

BEST COPY AVAILABLE

AIDS and on other new vaccines. There was more optimism that industry would be willing to produce certain vaccines on contract for situations where market size and vaccine safety and efficacy are not easily predetermined. Investment in the development phase when market size and vaccine safety and efficacy are not easily predetermined is too risky. As noted in Development (see pp. 6-7), the extent of the U.S. market could be predetermined if ACIP were to make prospective recommendations for a vaccine meeting its specifications. If the ACIP were to predefine the characteristics of the target populations, the industry could estimate sales based on the number of people fitting the profile.

The Army participant described the need to create links between the university scientists and the companies. This link is essential for achieving both development and production. At present only the Army has an aggressive program to overcome these barriers. The PHS has neither the funding nor the mandate to follow the pioneering efforts of the DOD.

The other incentive which received attention was that of increased patent protection and exclusivity for some period of time after a new vaccine reaches the market.

In the plenary session following the chairman's summary of the Production and Procurement working group, there was a discussion of special problems associated with development of improved vaccines where a licensed product already exists. First, if the product will not increase the market because it replaces or shares sales with an existing product, the incentive will not always be sufficient to fuel adequate R&D efforts. Pertussis was cited as an example where knowledge of adverse reactions significantly predated adequate investments in improving the vaccine. The public reaction has been translated into law suits, higher vaccine prices, shrinking of the industry and growing public concern about vaccine use, despite overwhelming data on the public health value of disease prevention.

The price of an improved vaccine will reflect the costs of large scale clinical trials to determine safety. Costs are also likely to include efficacy trials conducted abroad, because U.S. target populations have already been immunized with the older generation vaccines. There will be a U.S. licensing question about whether to allow an older product to maintain its license once a new improved version has been approved. There will be the ethical question about whether a less expensive, originally licensed vaccine or an improved more expensive one, will be purchased by UN programs for international consumption where the trade-off may be the number of children who will receive immunization.

Distribution and Use

This working group looked at the major impact of federal policy on national immunization rates. They cited federal purchase of vaccines for distribution to state and local health departments as a critical element in the success of childhood immunization programs. This mechanism currently accounts for 40-50 percent of all vaccines used in the U.S.

BEST COPY AVAILABLE

Concern was expressed about the erosion of positive effects of the federal purchase policy in three ways:

1. If the federal vaccine purchase budget does not increase and vaccine prices continue to rise, the number of doses distributed will be reduced. Incidence of preventable disease would rise, resulting in increased costs of treatment.

2. With fewer doses of essential vaccines available through state and local immunization programs, there is simultaneously a greater demand at public program sites (rather than in private physicians' offices). This session discussed the phenomenon of "dumping;" that is, the shifting of patients from private doctors to public programs in the same way that private hospitals are shifting patients to public medical facilities for treatment.

3. The failure to budget funds for a new vaccine in the federal purchase program although the medical indication is for widespread use. The example is the new Hemophilus influenzae type b vaccine which despite ACIP's recommendation for use, has not been included in the federal purchase program.

Two other aspects of federal policy were discussed and seen to be helpful, though less significant in controlling infectious disease. There is a great need for implementing an organized program for promoting the use of all, recommended adult vaccines. The attempt to increase use of pneumococcal vaccine by including it as a covered service under Medicare was viewed favorably, although this measure has not resulted in substantial increases in immunization rates so far. It was suggested that other adult vaccines such as influenza should also be covered by Medicare.

Consolidated vaccine purchase by states based on federal negotiations brought down the price of H. influenzae type b vaccine considerably. This approach was credited with improving the distribution and use of the new vaccine, although not as effectively as inclusion in the federal program of purchase might have been.

This group called for public education efforts on the value of immunization and disease prevention. Recent news about vaccines has been negative and damaging to public acceptance. Despite the media attention to problems associated with the pertussis vaccine, childhood immunization programs have been very successful in reducing rates of vaccine preventable disease.

There are still isolated pockets where children are not immunized despite school entry laws. Disease outbreaks remind us that our programs are not fully effective. The per child cost of reaching the isolated groups would be relatively high, but some of these children are precisely the ones who are at high risk.

This group spoke in favor of seeking to reach children before school entry age whenever possible. Day care was listed as the principal point of access for immunization as well as for exposure to infectious agents.

In contrast to the relative success with pediatric immunization is the experience with adults, particularly influenza and pneumococcal vaccines. The participants agreed that where the need for a vaccine

BEST COPY AVAILABLE

is not perceived by the public or by health professionals, or where the vaccine is problematic, the rate of use is poor. In addition to public education there was a call for "good, clean clinical trails" to clarify further questions of efficacy and safety.

Dramatic improvement in immunization rates among all populations can be achieved through organized programs. Data show that a well organized program can increase coverage of the target population from 10-20 percent up to 60-70 percent. The response to a range of organized programs, from a very sophisticated computer reminder to a simple campaign operated without any technology at all, is good. The chairman reiterated that the key elements were purposefulness and organization.

The group reviewed and supported all the uses of incentives and disincentives of which they were aware, and suggested some additional ones. Existing examples are: the school (and in some states, day care) entry laws; National Health Service Corps; continued funding contingent on immunization levels; and Indian Health Service administrative personnel performance evaluations based on immunization rates.

Additional opportunities put forward include: use of the peer review mechanism in Medicaid and Medicare; a mechanism of "informed refusal" which would require a doubter to pay a penalty should s/he contract a disease after shunning a recommended shot; and job or site transfer in the case of a worker's refusal to be immunized where s/he having refused immunization may be a disease carrier to high risk populations. This would apply particularly to health care workers in nurseries, nursing homes, etc.

Finally, this session expressed strong support for research on immunization practices to determine the characteristics of successful and unsuccessful programs and dissemination of the information that is available to improve these programs. It was pointed out that CDC gathers some useful annual information which needs to be better distributed. One participant noted that some of the research to obtain critical data could be appropriately supported by the Health Care Financing Administration (HCFA) and the National Center for Health Statistics Research (NCHSR) as well as by CDC.

Surveillance and Monitoring

This group discussed the uses of data, priority setting for optimal allocation of resources devoted to surveillance and monitoring, and identified some of the important gaps in our current data base.

Data provide the basis for evaluating disease incidence and prevalence and the associated costs, and for evaluating vaccines and immunization programs.

Good data provide the basis for sound policy decisions for both the government and industry. Policy makers can determine what can be achieved by effective disease prevention, the most beneficial new products, the size of the potential market, and the safety and effectiveness of existing vaccines.

The participants noted that it is currently very difficult to obtain accurate data on disease burden, citing the experience of the IOM committee in preparing the report on New Vaccine Development: Establishing Priorities, Volume 1 (1985). For example, CDC does not

BEST COPY AVAILABLE

collect national data on some diseases including respiratory infections by agent.

It was agreed that CDC should take the lead in setting priorities for data collection and analysis. A number of other groups can contribute. These include:

- o National Center for Health Statistics (NCHS), which independently collects information in interview surveys on immunization levels, disease occurrence and disability
- o NIAID, which can play a major role in epidemiologic studies of disease etiology and natural history
- o FDA, which monitors some data on adverse effects: it collects reports from manufacturers, pharmacists, physicians, and the military
- o state and local health officers who collect data related to school entry laws and pass it along to CDC
- o CDC which also receives reports by parents and guardians of children who receive federally funded vaccines
- o manufacturers, who receive reports about their vaccines
- o physicians who are asked by the FDA and state health departments to report certain disease and immunization reactions.

The group reported that significant gaps exist both from the point of view of the public health community and industry. As no catalog of available data has been assembled the group could give only examples and recommend that a thorough effort be undertaken to (1) list data needs; (2) compare this to the full range of data sources; (3) identify gaps; and (4) set priorities. They propose that this be part of a grander scheme to inform and coordinate vaccine and immunization efforts nationwide.

One example cited of existing problems was the uncertainty among private doctors about to whom to report which kinds of information. It was agreed that this confusion affects the utility of the entire data base because doctors in private offices give about 50 percent of all vaccines and are responsible for an even larger share of diagnosis and treatment of infections.

Another central issue is the lack of coordination in information collection, exchange and analysis between CDC, FDA, NIH, state and local health departments and vaccine manufacturers. It was noted that such communication is hindered by legal issues associated with protecting patient confidentiality as well as by bureaucratic barriers.

Much of the reporting is voluntary rather than mandatory; participants said the existing data base can be useful without being complete. Similarly, since states decide which diseases are reportable to CDC, the data base is not comprehensive and may lack particularly significant disease information. Both of these issues need to be reviewed.

As did the Development group, the Surveillance and Monitoring working group emphasized the essential and integral nature of data collection and analysis for a nationwide vaccine and immunization strategy.

This session concluded its presentation to the plenary session by stating its support for a coordinating body to assess the value of different sorts of data to (1) improve all aspects of disease, vaccine and immunization program data; (2) set priorities; and (3) seek to remove the barriers to full public health use of this science of

BEST COPY AVAILABLE

disease prevention. The approaches to be used could not be suggested without engaging in a thorough analysis of the existing data system and knowing something about the level of resources available to improve these functions.

Conclusion

In addition to recounting the substance of the workshop, it is important to report on the quality of the environment created by participants from all sectors. All sessions were characterized by pursuit of many possible approaches to improve all vaccine and immunization activities with a clear focus on the public health goals; no approach was foreclosed. There was a remarkable degree of openness in most of the discussions.

The deliberations ranged across ways of supporting and expanding industrial development and manufacture, university participation in clinical testing, private provider support for immunization, and government activities in all phases. Throughout the emphasis was on looking at all options, and seeking coordination for the overall effectiveness of the programs. New and closer arrangements between industry, government, and academia were discussed at length. Two efforts at greater coordination were discussed at the end of the plenary session (one ongoing and one historic). Dr. Gary Noble from CDC who chairs the existing interagency committee to coordinate governmental vaccine and immunization activities summarized their progress in working toward a better pertussis vaccine and stabilization of the supply of the existing vaccine. In response to a question from Dr. D.A. Henderson, he noted they have not yet found time to do similar planning or coordination for any of the new vaccines. There was no indication that that body has the staff support to perform the broader function of anticipating how to make optimal use of the new science. Dr. Gene Stollerman summarized the work of the Armed Forces Epidemiological Board which was once an active model of cooperation that subsequently lost its momentum when not operating in a wartime setting.

Dr. Helms, staff to the Senate Committee on Labor and Human Resources, was the last speaker called on by the chair. His remarks indicated the bipartisan nature of the concern for effective mechanisms for taking advantage of the new technology to prevent infectious disease, particularly given the overwhelming cost/benefit potential of immunization. He noted that the workshop had produced a range of ideas, including disagreements about possible solutions. In this process he saw the prospect for those of varying political persuasions to recognize the complexity of the task and to work together productively.

Dr. Henderson closed by congratulating the group on its responsiveness to the need to for innovation in taking advantage of the new age of vaccines for preventing infectious disease.

BEST COPY AVAILABLE

Congress of the United States

Washington, D.C. 20515

March 6, 1986

Samuel O. Thier, M.D., President
The Institute of Medicine
National Academy of Sciences
2101 Constitution Avenue, N.W.
Washington, D. C. 20418

Dear Dr. Thier:

We are writing to ask that the Institute of Medicine use its good offices to perform an important task for the Congress. The Institute has produced two important reports on vaccines and the prevention of infectious disease (and a third is now in press). These reports have contributed a great deal to our understanding of what can be accomplished with vaccines and some of the obstacles which hinder their development.

The revolution in biotechnology makes it possible to contemplate new and improved vaccines that would become available very quickly if research, development, and production were to go forward rapidly. However, we also know that this is not happening: competition for limited research funds and reluctance on the part of the vaccine makers to invest in new vaccines retard these advances.

There is now great interest in both Houses of Congress in legislation that would remove one impediment to new vaccine development -- concern over liability for injury caused by vaccines. This legislation may be enacted, and this would help protect the current vaccine supply. We are writing, however, because we believe that the United States needs an organized program to assure full benefit from new and improved vaccines. New vaccines and vaccines requiring improvement identified in the Institute's first report must be encouraged through research, development, clinical trials, licensing, and production into full use.

The Institute has already provided a sound analysis of the utility of the science in its previous vaccine studies. Now we need to examine specific mechanisms to achieve disease prevention goals with vaccines. We hope you might be able to convene a conference in the near future, where experts and interested parties would discuss the problem. We ask that you address the following questions concerning research, development, testing, supply, and use of vaccines:

1. What mechanisms must be created to assure that the research needed to invent cost-effective vaccines against human infectious disease is conducted either with government support or by private industry? This refers to the basic and applied research necessary to design and manufacture a vaccine. How will priorities for research be set and the research implemented?

BEST COPY AVAILABLE

2. What mechanisms are needed to assure development of new and improved vaccines? At the stage that a candidate vaccine is considered testable, a laboratory must produce sufficient quantities to carry out clinical trials and refine manufacturing methods. Both the Department of the Army and the National Institute for Allergy and Infectious Disease now collaborate with industry in vaccine development. The industrial base for such efforts needs to be fostered.

3. What procedures and programs are needed to assure that large scale clinical trials are conducted expediently on vaccines that are ready for such testing? Vaccine development is often halted at this stage. Field trials are expensive and it is often difficult to find a large enough population to test different doses, schedules and adjuvants. Assistance from the Food and Drug Administration's Office of Biologics would be helpful in designing clinical trials. This may be especially difficult logistically when testing outside the United States seems most appropriate.

4. When a vaccine is licensed for manufacture and sale, what kind of a program is needed to assure that an adequate supply is available to vaccine users? At present, the Federal government buys about one-half of certain pediatric vaccines to assure that they are available to public health programs. Can continued Federal procurement guarantee a supply of each vaccine that is cost-effective for preventing disease?

5. How can the programs in states and at the Centers for Disease Control that assure use of pediatric vaccines that are cost-effective be expanded to all vaccines in the U.S.? Innovative programs to reach adults are needed. This is the final element in a national program to guarantee optimum benefit from vacccines.

We are very pleased with the work of the Institute on vaccine policy. We believe that the full benefit of the effort will come with the enactment of a national program to assure optimal use of the new vaccine technology. Thus, we are asking you to tackle the most important remaining questions about vaccine research, development, testing, production, and use. The staff of the House Committee on Energy and Commerce and the Senate Committee on Labor and Human Resources will be available to work with the Institute if you find yourselves able to undertake this project.

Sincerely yours,

John D. Dingell
Chairman
House Committee on Energy and Commerce

Orrin G. Hatch
Chairman
Senate Committee on Labor and Human Resources

BEST COPY AVAILABLE

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

SAMUEL O. THIER
PRESIDENT

April 17, 1986

Anthony C. Allison, M.D., Ph.D.
Vice President and Director
Institute of Biological Sciences
Syntex Research
3401 Hillview Avenue
Palo Alto, CA 94303

Dear Dr. Allison:

I am writing to formally invite you to participate in a two-day workshop on vaccine innovation and supply to be held at the National Academy of Sciences on April 24-25, 1986.

The workshop will be convened in response to a request from Representative John D. Dingell (D-Michigan), chairman of the Committee on Energy and Commerce, and Senator Orrin G. Hatch (R-Utah), chairman of the Committee on Labor and Human Resources. As you will see from their letter, a copy of which is attached, serious consideration is being given to enactment of a national program to assure optimal use of new vaccine technology.

It is our understanding that new legislation is being proposed in the area of liability and compensation for vaccine-associated injury. The need for legislative action in other areas is, however, also recognized. Hence, our workshop would extend previous efforts of the Institute of Medicine and consider specific mechanisms and needs in various key areas--research, development, testing, supply, and use. Further details of the charge to the workshop and the agenda will be sent to you shortly by Roy Widdus, Director, Division of International Health, and Phyllis Freeman, an Institute of Medicine scholar-in-residence, who are working together on the project.

We are pleased that you are willing to spare the time to help guide this national effort in vaccine policy formulation.

With best wishes,

Sincerely,

Samuel O. Thier, M.D.

Enclosure

BEST COPY AVAILABLE

INSTITUTE OF MEDICINE

WORKSHOP ON VACCINE SUPPLY AND INNOVATION

April 24-25, 1986

Room 451, Joseph Henry Building
2100 Pennsylvania Avenue, N.W.
Washington, D.C.

AGENDA

Thursday, April 24

9:30 - 9:45	Opening Remarks and Charges to the Working Groups - Dr. Samuel O. Thier, President, Institute of Medicine
9:45 - 10:15	Introduction to the Problem: A Congressional Perspective - Dr. Anthony Robbins, Professional Staff, Committee on Energy and Commerce
10:15 - 10:30	Questions and Answers
10:30 - 10:45	Break - Working Groups Reconvene in Individual Rooms
10:45 - 12:30	Working Groups Meet: Set Agenda, Start Discussions
12:30 - 1:20	Lunch
1:20 - 5:00	Reconvene in Individual Rooms
5:00	Adjourn

Friday, April 25

8:30 - 10:15	Reconvene - Plenary Session, Room 451 - Dr. Donald Henderson, Chairman
10:15 - 10:30	Break
10:30 - 1:00	Reconvene - Plenary Session, Room 451
1:00	Adjourn

BEST COPY AVAILABLE

OPENING REMARKS OF DR. SAMUEL O. THIER AT THE MEETING ON VACCINE SUPPLY AND INNOVATION

Good Morning, I am Samuel Thier, President of the Institute of Medicine. I am delighted to welcome you on behalf of Institute and thank you for your willingness to participate in this meeting, especially those of you that have received relatively short notice. We are particularly happy to see a number of individuals that were involved in the previous IOM studies on Vaccine Priorities and Vaccine Supply and Innovation.

This meeting is one example of how the Institute of Medicine and the National Academy of Sciences respond to that part of our charge to provide advice to the government. You have all received the letter from Congressman Dingell and Senator Hatch outlining their request to the IOM for advice. In both plenary session and in subgroups we will be extending the previous work of IOM committees. Some of you are familiar with this, but not all of you are; therefore, I will review those efforts briefly.

The Committee on Issues and Priorities for New Vaccine Development under the chairmanship of Dr. Samuel Katz, developed methods for setting priorities for accelerated vaccine development, both for diseases of importance in the United States and for diseases of importance in developing countries. That group did valuable work in devising a method by which the incidence, health effects and costs of infectious diseases can be compared against each other. The method they devised incorporates not only data on the numbers of cases, complications and sequelae of various diseases in different age groups, but also can take into account more subjective, value judgments on the relative undesirability of disease conditions. As well as being part of the process of setting priorities for accelerated vaccine development the method that the committee devised for disease comparison could possibly be used to assist in deciding long term research priorities.

The Committee on Public-Private Sector Relations in Vaccine Innovation, chaired by Dr. Jay Sanford, explored many issues similar

BEST COPY AVAILABLE

to those we will be discussing today, but it focussed predominantly on the organizational issues and questions surrounding liability and compensation for vaccine related injuries. The liability issue is one which we are setting aside for the purposes of today's discussions. In regard to the organization of vaccine innovation in the United States, that committee recognized the scientific strength that has made the U.S. a leading force in vaccine innovation over the last 2 or 3 decades. In considering solutions to improving vaccine supply and innovation it worked from the premise that we should utilize and build on the strengths of existing government agencies and the industry.

At the same time the committee felt that there was a need to bring cohesion to the country's vaccine innovation efforts. This seems to be a focal point in the letter from Chairmen Dingell and Hatch as well. Our committee discussed the advantages and disadvantages of locating this force for cohesion in various places within the government (either the executive or legislative branches) or outside the government (either attached to an existing institution or a free standing new body). The committee recommended a private nonprofit corporation, but this recommendation was made in part because previous recommendations for the creation of such a body within the government had been neglected. The committee's fundamental belief was that, such a body or commission could usefully serve its purpose in a variety of locations, not any one of which would be totally perfect.

We are gathered here today to take that recommendation another step toward reality. We expect to examine some of the specific mechanisms that would need to be put in place for a commission or the coordinating body to fulfill its functions most effectively. We will begin by examining a variety of issues in subgroups; however, it will be useful when you are in working groups to bear in mind some of the broad functions that the Committee on Public-Private Sector Relations felt were most lacking in the present organizational arrangements:

1) identifying production problems and commercial decisions that pose a threat to vaccine supply
2) determining the need for improving existing vaccines

BEST COPY AVAILABLE

3) monitoring vaccine innovation activities o see that they reflect public health needs

4) monitoring vaccine needs for developing countries and promoting efforts to meet these needs

5) evaluating biotechnological advances that could potentially hasten progress in vaccine innovation and production

6) promoting and evaluating efforts designed to increase knowledge of public health benefits of immunization programs and participation in them. (There are available techniques which should enable us to design better immunization programs, but these by and large have not been incorporated into educational efforts.)

7) monitoring the supply and training of specialized personnel necessary for vaccine innovation. (In particular, do we have a sufficient supply of people knowledgeable in industrial processes involved in vaccine production?)

8) monitoring and evaluating legal issues that effect vaccine development and use.

You can discuss in the plenary session Friday how the activities in different areas may be best tied together.

I would end my comments by stressing that the activities of the Institute of Medicine, particularly those of the committee on Public Private Sector Relations in Vaccine Innovation, have attempted to develop ideas which would complement rather than replace the system which exists in this country for vaccine research, development, production, supply and use. There are both strengths and gaps in that system but the challenge to you today is to make suggestions to identify ways to strengthen further what we have and make its parts fit into a more cohesive whole -- a system the nation can understand and rely upon. We want to take full advantage of the new techniques available for making vaccines, so there will surely be some new elements to add to our national capacity in the coming years.

The format of this meeting is designed to stimulate the broadest possible identification of the various ways in which barriers to

BEST COPY AVAILABLE

vaccine development and use can be overcome. We will not be striving for consensus that any one of these particular solutions is the most appropriate. In many instances the selection of the most appropriate way of overcoming a barrier or deterrent involves consideration which are inherently political and we should leave such balancing to the politicians. Our task is to identify the mechanisms which could be used to improve the situation and their pros and cons.

I look forward to a productive and useful meeting.

BEST COPY AVAILABLE

REMARKS BY ANTHONY ROBBINS, M.D.
APRIL 24, 1986
INTRODUCTION TO THE PROBLEM
A CONGRESSIONAL VIEW

The Congress needs help in setting new national policy for research, development, production, and use of new and improved vaccines. Chairmen Dingell and Hatch have chosen to come to the Institute of Medicine for help with the major, long-term policy questions: What kind of program is needed to assure that the United States (and the world) receive optimum benefit from vaccines in preventing human disease? In coming to the Institute of Medicine, they dispatched their request to the right place. The Institute's first report on vaccines -- New Vaccine Development -- Establishing Priorities -- recognized the new potential in vaccines. There is new knowledge of disease processes, pathogens, and host responses. Biotechnology can revolutionize the development and production of vaccines. The report built on the analyses by the National Institute for Allergy and Infectious Disease to set priorities for vaccine research and development. The second volume, in particular, reflects the rapid growth in the ability of health authorities and professionals around the world to make use of new and improved vaccines in developing countries.

The Institute's vaccine innovation report reflects a certain disappointment that the United States currently seems unable to take full advantage of the advances in vaccine technology. The immediate vaccine supply is in jeopardy, chiefly because of the reluctance of industry to sell vaccines in the legal climate created around vaccine injuries. Thus, the IOM's policy suggestions are complete and detailed on the issues of injury, liability, and compensation.

Chairman Dingell and Senator Hatch were alert to the IOM's activities when they wrote to Dr. Thier. (Please note that the Congress does pay attention to IOM reports.) Thus, it is with full knowledge of these reports that the Chairmen requested the

BEST COPY AVAILABLE

IOM's help on a long-term problem that was not already covered in sufficient detail. Today's question is how to bring U.S. vaccine research, development, production, and use into line with the opportunities inherent in today's science and into line with the public health needs of the Nation. (Many of my colleagues from congressional staffs are here today to hear the discussions.)

Vaccine injury, liability, and compensation are hot issues. They have caught the interest and imagination of many in the Congress. They have engaged many powerful interests with their retinue of lobbyists. They do cry out for a legislative remedy. But that is not why we are here today! Today we must address a more basic and lasting problem -- a problem that will not be solved by addressing the issues of injury, liability, and compensation. Throughout the continuing debate on these issues, no one has suggested that a remedy to these acute legal problems will create an adequate and reliable program to prevent disease using new and improved vaccines.

It is this unspoken consensus that has brought the Congress back to the IOM. Can you help the Congress understand the issues and design the future program for research, development, and use of vaccines and immunization to prevent human disease? For if the Congress understands the need for an organized program, it should be possible to mandate it at the same time that vaccine liability remedies are legislated. I believe that this question is aimed directly at the strength of the IOM.

* * *

There is a rich tradition in vaccines in our biomedical research and public health communities. There is a history of analysis, programs, and campaigns, and a vast wealth of personal experience that makes the design of a national vaccine program possible. This collective wisdom is assembled here today!

- The National Institute for Allergy and Infectious Disease has displayed prescience on vaccine research, but Bill Jordan can describe some of the frustrations that come with thinking ahead.
- The Centers for Disease Control, the Advisory Committee on Immunization Practice, the Academy of Pediatrics, and the

BEST COPY AVAILABLE

American College of Physicians have contributed mightly to widespread and proper use of vaccines.

- The Food and Drug Administration's Office of Biologics has produced both research and a credible program of licensure.

- Industry, which has developed many of our best vaccines, is well represented today. Its participants include some of the great heroes and veterans of the vaccine world: Maurice Hilleman and Ben Rubin.

- The Army heroes are here too. They continue their work in the massive Department of Defense even though their budget is so relatively small their superiors often overlook it as a rounding error.

- The research teams of our universities are also here.

- The Agency for International Development, which has consistently supported vaccines as part of effective foreign aid, is well represented.

- The United Nations and its agencies are here, and many veterans of international efforts, such as the chairman for the plenary session, D. A. Henderson.

There is danger as well as strength in this assemblage. You each have concerns and many have special interests, but few have devoted their best efforts to looking at the continuum from research to production, use, and surveillance. The vaccine world as seen by R&D folks is very different than that as seen by the public health people concerned with distribution and use. This conference must get beyond each element to see the whole picture and design an overall plan or program.

* * *

It is probably useful to understand why the Congress requested this workshop now. I believe there is a very real opportunity to apply the collective experiences to Congressional deliberations if they can be captured today. Congress is already focused on vaccines: the injury issue, the threat to the current supply, and the work of the international campaign to immunize all children by the year 1990. If the Congress chooses to legislate on these issues, why not do the job correctly and

BEST COPY AVAILABLE

create a program to assure effective research, development, production, and use of vaccines.

I have spoken with many of you and many others. Everyone has been helpful in dissecting the process. Some have described research opportunities. Others have told of development obstacles, and still others of problems faced is getting vaccines to the people. The indivdual steps are becoming clear. It is the way to tie them together that is missing. The plan should be prospective, looking several years ahead. It should make all of the elements of a vaccine program predictable, including the role of industry in each particular vaccine.

In the absence of an overall plan and overall responsibility, there are too many individual steps; with each capable of becoming an obstacle or bottleneck. We need a plan. Indeed, we probably need a plan with contingency plans, back-up, and some redundancy.

We have just started to draft legislation to create the plan and program and to assure continuity. Let me describe this early thinking briefly. I will gladly share with anyone our first sketchy draft.

The legislation would create a small unit, a secretariat or administrative group, responsible for all human vaccine research, development, trials, licensing, production and procurement, distribution and use, and surveillance. This management unit would have one key product, an annual national plan, incorporating all vaccine activities within the Public Health Service, U.S. AID, and the DOD (except biological warfare efforts). It would take full account of activities in industry. The plan is the critical element for avoiding delays and assuring continuity. A review of research would describe what vaccines can and should move to development. Future clinical trials and licensing review would be spelled out in the plan. Production resources would be described, as would how users will acquire the vaccines. The systems that will be used to distribute vaccine to the right population will also be included. Monitoring and surveillance, used to guide future plans, would be required.

BEST COPY AVAILABLE

Throughout the plan, the resources needed to do each task would be specified.

The director of the program would be responsible to the Congress for the annual plan and responsible for achieving its prioritized goals to the extent of the resources provided. With a plan in place, existing agencies would continue as the operating arms of the plan, with a some additional funds available to the Director to overcome unexpected developments in any part of the plan that might endanger its overall success.

The Director would work with two groups to produce the plan, an interagency committee of all relevant government agencies, and an external group with representatives of industry, state and local government, professionals, and citizen groups.

It all seems very simple, but I believe that it supplies the missing element that currently blocks adequate Congressional support for vaccines and immunization: the ability to visualize the public health results as soon as the research results start to materialize. These projections of tangible outputs can attract appropriate funding because the benefits can be clearly delineated. The Congress will invest in the future where the payoff is evident.

The IOM has organized the conference in a way that should be exceptionally helpful to the Congress. It allows the conference to note and perserve what is good today and to design what is needed to make the system whole. Thus each piece is discussed and the whole assembled:

- The first group asks how to assure attention to the best research opportunities.
- The working group on development is asked to figure out how to assure that research results lead to investment in vaccine development, either private or government.
- The group on clinical trials can tell us how to eliminate the current obstacles that slow development at the point of needing clinical tests.
- Licensure, partly because it is the creature of the Congress, deserves special attention to make sure that the FDA

BEST COPY AVAILABLE

role is appreciated and geared to helping make better use of vaccines.

- The fifth group, on production and procurement, must define the future roles of government and industry. Physical and scientific resources of both must be considered, and the working group must be open to new kinds of cooperation and collaboration to meet public health objectives. Industry and government must be reliable partners.

- The working group on distribution and use is charged with discussing how to enhance programs that make use of vaccines. This includes critical issues of public education and how to be as successful with adult vaccines as we are with children.

- Finally, the group on surveillance and monitoring is being asked to discuss how these activities can give us confidence in the planning and decision-making that will guide all of the other activities.

For each area we ask you to keep an eye on the needs of international immunization programs so that the U.S. can contribute to the most effective public health efforts in the world.

If all this is asked of you, it is fair to ask what is the Congress doing? I believe that there are three useful attitudes inherent in the letter from the chairmen. First, they ask tough questions and will listen to the response. Congress sees both problems and opportunities. It is confronted with facts, but has not been presented with solutions for the future. For example, we may need manufacturing facilities that can produce many different vaccines. We may need small batches of special vaccines for special populations. Congress needs to hear that these kinds of problems are soluble. There is no expectation of universal consensus, rather an airing of the big issues. Second, the Chairmen do not accept any glib assertions that the problem of vaccines will take care of itself. Third, they will demand a plan and a program of vaccine activities--governmental, industrial, and academic--so that Federal money is spent well and achieves the desired results.

BEST COPY AVAILABLE

WORKING GROUP MEMBERS

Room 358	Room 454	Room 357	Room 451	Room 455	Room 354	Room 750
Research	Development	Clinical Testing	Licensing	Production and Procurement	Distribution and Use	Surveillance and Monitoring
WARREN*	SMITH*	KATZ*	STOLLERMAN*	HENDERSON*	PERSON*	CHIN*
Allison	Curlin	Cano	Barry	Beale	Hinman	Brunell**
Berns	Elliott	Clements	Ennis	Gilmartin	Johnson	Feldman
Chanock	Gallin	Cotton**	Faber	Grady	Mather	Freilich
Choppin	Gonzalez-Pacheco	de Quadros	Goyan	Hardy	Nickerson	Kiltie
Feinberg**	Groves	Francis	Lepow	Rathmann	Scott	Kothe
Jordan	Hill	Gordon	Mike**	Richmond	Watson**	Lampe
Lasky	Hilleman	Halsey	Rubin	Robinson		
Moss	Lawton	Hanclark	Schultz	Sadarini		
Quinnan	Metzgar	Melnick		Sanford		
	Noble**	Stevens		Shelokov		
	Obijeski	Ward		Sisk**		
				Van Dusen		
				Wilcox		
				Williams		
				Yetter		

*Chairmen
**Notetakers

APPENDIX 6

BEST COPY AVAILABLE

INSTITUTE OF MEDICINE

WORKSHOP ON VACCINE SUPPLY AND INNOVATION

April 24-25, 1986

ATTENDANCE

Anthony C. Allison, M.D., Ph.D.
Vice President and Director
Institute of Biological Sciences
Syntex Research
3401 Hillview Avenue
Palo Alto, CA 94303
(415) 855-5050

David Barry, M.D.
Vice President of Research
Wellcome Research Laboratories
Burroughs Wellcome Company
3030 Cornwallis Road
Research Triangle Park, NC 27709
(919) 248-3000

John Beale, M.D.
Wellcome Research Laboratories
Langley Court
Beckenham, Kent
BR3 3BS
United Kingdom
011-44-1-658-2211

Kenneth Berns, M.D.
Chairman
Department of Microbiology
Cornell University School of Medicine
1300 York Avenue
New York, New York 10021
(212) 472-5454

Phillip A. Brunell, M.D.
Professor and Head
Division of Infectious Diseases
University of Texas Health Science Center
7703 Floyd Curl Drive
San Antonio, TX 78284
(512) 691-7116

Francis R. Cano, Ph.D.
Manager, Biologicals
Lederle Laboratories
Pearl River, NY 10965
(914) 735-5000 x3120

Robert M. Chanock, M.D.
Chief
Laboratory of Infectious Diseases
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 7, Room 100
9000 Rockville Pike
Bethesda, MD 20205
(301) 496-2024

James Chin, M.D.
Chief, Infectious Disease Section
State Department of Health Services
2151 Berkeley Way, Room 708
Berkeley, CA 94704
(415) 540-2566

Purnell W. Choppin, M.D.
Vice President and Chief Scientific Officer
Howard Hughes Medical Institute
7984 Old Georgetown Road
Bethesda, MD 20814
(301) 654-4020

Mary Lou Clements, M.D.
Director
Center for Immunization Research
Department of International Health
Johns Hopkins University
School of Public Health
615 North Wolfe Street
Baltimore, MD 21205
(301) 955-4054

BEST COPY AVAILABLE

George T. Curlin, M.D.
Associate Director for International Health Research
Office of International Health
Fogarty International Center
National Institutes of Health
Building 38A, Room B2N13
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-2516

Ciro C.A. de Quadros, M.D.
Regional Advisor
Expanded Programme on Immunization
Pan American Health Organization
525 Twenty-third Street, N.W.
Washington, D.C. 20037
(202) 861-3247

Arthur Y. Elliott, Ph.D.
Director
Biological Manufacturing
Merck Sharp & Dohme
West Point, PA 19486
(215) 661-6072

Francis A. Ennis, M.D.
Professor of Medicine and Molecular Genetics
University of Massachusetts Medical Center
55 Lake Avenue, North
Worcester, MA 01605
(617) 856-4182

Elaine C. Esber, M.D.
Director
Office of Biologics Research and Review
Food and Drug Administration
6600 Fisher Lane
Rockville, MD 20857
(301) 443-2544

David S. Fedson, M.D.
Head, Division of General Medicine
Department of Medicine
University of Virginia School of Medicine
Charlottesville, VA 22908
(804) 924-1935

Jacob Feldman, Ph.D.
Assistant Director for Analysis and Epidemiology
National Center for Health Statistics
3700 East-West Highway, Room 2-227
Hyattsville, MD 20782
(301) 436-7026

Donald P. Francis, M.D., D.Sc.
AIDS Advisor
Infectious Disease Branch
Department of Health Services
California State Health Department
2151 Berkeley Way, Room 708
Berkeley, CA 94704
(415) 540-2879

William Freilich
Legal Counsel
Merck Sharp & Dohme
West Point, PA 19486
(215) 661-6122

John Gallin, M.D.
Director, Intramural Research Program
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 10, Room 11C103
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-3006

John Gilmartin
Procurement Officer
United Nations Children's Fund
866 United Nations Plaza
New York, NY 10017
(212) 415-8000

Mario Gonzalez-Pacheco, Ph.D.
Regional Advisor in Biology
Pan American Health Organization
525 Twenty-third Street, N.W.
Washington, D.C. 20037
(202) 861-3216

BEST COPY AVAILABLE

Lance K. Gordon, Ph.D.
Senior Research Scientist
Connaught Research Institute
1755 Steeles Avenue West
Willowdale
Ontario
Canada M2R 3T4
(416) 667-2609

Jere E. Goyan, Ph.D.
Dean
School of Pharmacy (S926)
University of California
500 Parnassus Avenue
San Francisco, CA 94143
(415) 476-1225

George F. Grady, M.D.
Assistant Commissioner for Laboratories and Communicable Disease Control
Massachusetts Public Health Biologics Laboratories
375 South Street, Jamaica Plain
Boston, MA 02130
(617) 522-3700

Colonel Michael Groves
Director
Military Disease Hazards Research Program
Headquarters
U.S. Army Medical Research and Development Command
Ft. Detrick
Frederick, MD 21701-5012
(301) 663-7567

Neal Halsey, M.D.
Director
Division of Disease Control
Department of International Health
The Johns Hopkins School of Hygiene and Public Health
615 N. Wolfe Street, Room 5515
Baltimore, MD 21205
(301) 955-3934

George E. Hardy, M.D.
Assistant Director
Centers for Disease Control
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Room 728-F
Washington, D.C. 20201
(202) 245-8598

Donald A. Henderson, M.D.
Dean
School of Hygiene and Public Health
The Johns Hopkins University
615 N. Wolfe Street
Baltimore, MD 21205
(301) 955-3540

James C. Hill, Ph.D.
Assistant to the Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A04
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-9088

Maurice R. Hilleman, Ph.D., Sc.D.
Director
Merck Institute for Therapeutic Research
Merck Sharp & Dohme Research Laboratories
West Point, PA 19486
(215) 661-6352/5532

Alan R. Hinman, M.D.
Director
Division of Immunization
Center for Prevention Services
Centers for Disease Control
1600 Clifton Road, N.E.
Atlanta, GA 30333
(404) 329-1880

BEST COPY AVAILABLE

Pamela Johnson, Ph.D.
Child Survival Coordinator
Office of Health
U.S. Agency for International Development
Room 709, SA-18
Department of State
Washington, D.C. 20523
(202) 235-8926

William Jordan, M.D.
Director, Microbiology and Infectious Diseases Program
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 31, Room 7A52
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-1884

Samuel L. Katz, M.D.
Wilburt C. Davison Professor and Chairman
Department of Pediatrics
Duke University Medical Center
Box 2925 - Pediatrics
Durham, NC 27710
(919) 684-3734

Harriet Kiltie, M.D.
Medical Director
Lederle Laboratories
Middletown Road
Pearl River, NY 10965
(914) 735-5000 x3673

Martha Kothe, Ph.D.
Research Associate
Bruener Foundation, Inc.
132 West 43rd Street
New York, NY 10036
(212) 719-3110

Kenneth Lampe, Ph.D.
Chairman
Department of Drugs
American Medical Association
535 N. Dearborn Street
Chicago, IL 60610
(312) 645-4559

Larry Lasky, Ph.D.
Senior Scientist
Department of Molecular Biology
Genentech, Inc.
460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 266-1123

Stephen E. Lawton, Esquire
Pierson, Ball and Dowd
1200 18th Street, N.W., 10th Floor
Washington, D.C. 20036
(202) 457-8639

Martha L. Lepow, M.D.
Professor of Pediatrics
Department of Pediatrics
Albany Medical Center College
43 New Scotland Avenue
Albany, NY 12208
(518) 445-3125

Charles R. Manclark, Ph.D.
Chief, Pertussis Laboratory
Division of Bacterial Products
Office of Biologics Research and Review
Food and Drug Administration
Building 29, Room 418
8800 Rockville Pike
Bethesda, MD 20892
(301) 496-5564

BEST COPY AVAILABLE

Susan Mather, M.D., M.P.H.
Program Chief for Pulmonary and Infectious Diseases
Medical Service (111)
Veteran's Administration
810 Vermont Avenue, N.W., Room 915
Washington, D.C. 20420
(202) 389-2450

Joseph L. Melnick, Ph.D.
Distinguished Service Professor of Virology and Epidemiology
Baylor College of Medicine
Houston, TX 77030
(713) 799-4443

Donald P. Metzgar, Ph.D.
Vice President of Operations
Connaught Laboratories, Inc.
Swiftwater, PA 18370
(717) 839-7187 x208

Larry Miike, M.D., J.D.
Senior Associate and Project Director
Office of Technology Assessment
U.S. Congress Health Programs
Washington, D.C. 20510
(202) 226-2070

Bernard Moss, M.D.
Chief, Laboratory of Viral Diseases
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Building 5, Room 316
9000 Rockville Pike
Bethesda, MD 20892
(301) 496-9869

Gary Nickerson
20th Century Fund
41 East 70th Street
New York, NY 10021
(212) 535-4441

Gary Noble, M.D.
Assistant Director for Science
Centers for Disease Control
Building 1, Room 2047
1600 Clifton Road, N.E.
Atlanta, GA 30333
(303) 329-3701

Jack Obijeski, Ph.D.
Senior Director for Product Development
Genentech, Incorporated
460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 266-1255

Gerald V. Quinnan, Jr., M.D.
Director, Division of Virology
Office of Biologics, Research and Review
Center for Drugs and Biologics
Food and Drug Administration
Building N29A
8800 Rockville Pike
Bethesda, MD 20892
(301) 496-3144

George Rathmann, Ph.D.
President
Amgen
1900 Oak Terrace Lane
Thousand Oaks, CA 91320-1789
(805) 499-5725

Julius B. Richmond, M.D.
Director
Harvard University Division of Health Policy Research and Education
641 Huntington Avenue, Room 316
Boston, MA 02115
(617) 732-1410

BEST COPY AVAILABLE

Colonel David Robinson
Project Manager, Biological Systems
Headquarters
United States Army Medical Research
and Development Command
Ft. Detrick
Frederick, MD 21701
(301) 663-7661

Benjamin Rubin, Ph.D.
Professor of Microbiology and
Public Health
Philadelphia College of Osteopathic
Medicine
4190 City Line Avenue
Philadelphia, PA 19131
(215) 581-6446

Ronald Saldarini, Ph.D.
Vice President
Lederle Laboratories
American Cyanamid Company
One Cyanamid Plaza
Wayne, NJ 07470
(201) 831-2000 x2208

Jay P. Sanford, M.D.
Dean, School of Medicine
Uniformed Services University
of the Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814
(301) 295-3013

William Schultz
Staff Attorney
Public Citizen Litigation Group
2000 P Street, N.W., Suite 700
Washington, D.C. 20036
(202) 872-0320

H. Denman Scott, M.D., M.P.H.
Director
Rhode Island Department of Health
75 Davis Street
Providence, RI 02908
(401) 277-2231

Alexis Shelokov, M.D.
Director of Vaccine Research
The Salk Institute
9200 Old Annapolis Road, Suite 201
Columbia, MD 21045
(301) 596-1960

Jane Sisk, Ph.D.
Project Director
Office of Technology Assessment
U.S. Congress Health Programs
Washington, D.C. 20510
(202) 226-2070

David H. Smith, M.D.
President
Praxis Biologics
300 East River Road
Rochester, NY 14623
(716) 424-7300

Cladd E. Stevens, M.D.
Investigator and Head
Laboratory of Epidemiology
The New York Blood Center
310 E. 67th Street
New York, NY 10021
(212) 570-3167

Gene H. Stollerman, M.D.
Professor of Medicine
School of Medicine
Boston University
720 Harrison Avenue, Suite 1108
Boston, MA 02118
(617) 638-8030

Ann Van Dusen, Ph.D.
Deputy Director of Health
Office of Health
U.S. Agency for International
Development
Room 709, SA-18
Department of State
Washington, D.C. 20523
(202) 235-8926

BEST COPY AVAILABLE

Joel I. Ward, M.D.
Director, Medical Epidemiology
Harbor - UCLA Medical Center
1000 W. Carson Street
Torrance, CA 90509
(213) 533-2345

Kenneth Warren, M.D.
Director, Health Sciences Division
The Rockefeller Foundation
1133 Avenue of the Americas
New York, NY 10036
(212) 869-8500 x320

William Watson
Project Manager
Task Force for Child Survival
1989 N. Williamsburg Drive
Suite I
Decatur, GA 30033
(404) 325-2452

Kenneth Wilcox, M.D., Dr.P.H.
Chief
Bureau of Laboratory and
Epidemiological Services
Michigan Department of Public Health
P.O. Box 30035
Lansing, MI 48909
(517) 373-1301

David J. Williams
Vice President and General Manager
Connaught Laboratories, Inc.
Swiftwater, PA 18370
(717) 839-7187 x213

Wayne Yetter
Senior Director of Marketing
Merck Sharp & Dohme
West Point, PA 19486
(215) 661-5607

Frank E. Young, M.D.
Commissioner
Food and Drug Administration
Room 14-71 Parklawn Building
5600 Fisher Lane
Rockville, MD 20857
(301) 443-1544

BEST COPY AVAILABLE

Working Group #1

RESEARCH

For the purpose of this working group research is defined as those activities intended to enhance our fundamental knowledge about diseases, pathogens, vectors, adjuvants, and host responses and thus make vaccine development possible. Although this is a broad definition of research, the IOM's report on vaccine development priorities demonstrates that for each vaccine preventable disease, it is possible to describe the specific research areas that will bring knowledge to the point of developing a particular vaccine.

As part of the National Institute for Allergy and Infectious Disease's program of Accelerated Vaccine Research and Development, and more recently from the IOM, we possess analyses of vaccine research that describe what can be accomplished and when. Basic research questions are listed in these plans. Priorities are proposed.

As descriptions of needed research have been created in the past, it seems possible that any national vaccine plan could contain a similar product. The work group's task is to describe how research needs and opportunities can be evaluated, prioritized, and the plan updated regularly.

Other questions inherent in the idea of a research plan are:

1. How can the research programs of government agencies (PHS, DOD and USAID) be complementary and minimize neglect of important research opportunities or unnecessary duplication?

2. How can the research resources of industry participate in a national research program?

3. Can the National Institutes of Health's program of investigator initiated research be enhanced by solicitation or by other means, to assure more complete coverage of research opportunities?

4. Does the presence of a research plan improve the chance to increase funds? From the Congress? From Industry?

5. How can such a research plan contribute to the disease prevention needs of developing countries and international efforts to immunize people around the world?

6. Would identification of priority public health research needs help academic researchers?

For the benefit of the Congress which requested this conference, it is important to spell out how to assure that government, universities, and industry can take full advantage of research opportunities to improve our ability to produce new, safer, and more effective vaccines.

BEST COPY AVAILABLE

Working Group #2

DEVELOPMENT

For the purpose of this working group, development can be defined as the use of research on a particular vaccine to produce it in test batches for clinical trials and, if they are successful, to address the engineering problems of scale-up to allow for industrial level production. Research that is needed to design a vaccine is often supported without detailed planning for the production, marketing, and use of the resulting vaccines. However, development is the first step where both government agencies and industry are clearly guided by analyses of future results, both financial and public health. A major investment occurs at this point.

The Appropriations Committee hearing transcripts are replete with examples of NIAID decisions not to proceed with the development contracts for lack of funding, and the industry reports hesitation at the point of investing in the development of specific vaccines.

In order to assure full use of research results and to avoid delays at the point of development, the working group's task is to evaluate the resources currently available to do vaccine development including the following questions:

1. Are the resources from government, industry and universities commensurate with development needs? Physical plant and professionals are critical, but may have atrophied.

2. Can the existing resources be coordinated to improve their effectiveness?

3. Is more government funding needed to assure consistent participation of industry and university resources? If so, what forms might additional funding best take: grants, subsidies, incentives, etc?

4. What role could a national vaccine program play to assure that the existence of a licensed vaccine for a particular disease does not deter subsequent improvements?

5. How can the guidelines and resources of a U.S. national vaccine program contribute to the development of high priority vaccines for developing countries and to international efforts to assist these countries?

Specifically, the working group should consider the roles of the PHS, the Army, and USAID which currently invest in vaccine development. It should discuss the role of the university centers. It should also assess various ways that the resources of private industry can play a consistent role in a national program of vaccine development. The Army has made the most complete review of this issue and NIH has become very concerned about how to conduct development activities on an AIDS vaccine.

BEST COPY AVAILABLE

Working Group #3

CLINICAL TRIALS

All new vaccines currently require clinical trials for safety and efficacy. It appears that concerns about the feasibility and cost of clinical trials may act as a deterrent to the development of otherwise promising vaccines. It is important that uncertainty about requirements of the FDA, foreign countries and international organizations not impede clinical trials or deter development. In addition, it is important that companies not used to dealing with the licensing process not be deterred from pursuing vaccines out of fear of the complexity of regulations.

The task for the working group is to (1) describe the conditions that cause clinical trials to be a bottleneck in the process of getting new vaccines to the population, and (2) lay out possible remedies for phases I, II, and III testing.

There already exists a commitment at FDA to make approval of useful products more rapid. The group should consider how a more formal commitment, as part of a national vaccine plan, could be described and implemented.

1. License applicants have commented that FDA deters their efforts by not indicating how results will be evaluated. Is there any way that standards for safety and efficacy can be set out before clinical trials begin?

2. How can populations, U.S. or abroad, be found for testing, so that results meet the requirements for U.S., foreign, and international organization approval?

3. Is there a need for helping small companies through the regulatory maze?

4. What are the problems of using data gathered abroad?

BEST COPY AVAILABLE

Working Group #4

LICENSURE AND QUALITY CONTROL

Licensing of a vaccine for use in the United States is largely in the control of a government agency. The industry can decide not to apply or not to proceed past investigative status to a license for marketing. There is no doubt that the independence of the Food and Drug Administration must be guarded carefully. However, the effectiveness of public health programs that use vaccines are clearly in jeopardy when the applicant for a high priority product is discouraged from proceeding at all or when the resources of the Food and Drug Administration are inadequate to respond to the need to review and license new vaccines in a timely fashion. The task for this work group is to figure out how the Office of Biologics can participate in national planning for vaccines. The goal is to assure that needed resources are available for reviews and that the makers of vaccines that have national priority receive counsel prior to review so that the process can be expedited.

There are several specific questions:

1. How can the Office of Biologics set its priorities to respond to national public health priorities for vaccines?

2. How can the FDA take advantage of a national plan for vaccines to conduct some of the work needed for safety and efficacy review prior to the receipt of a complete application?

3. How can collaboration on review activities with foreign governments and international organizations be enhanced?

4. Is it possible to project the funds and other resources that will be necessary for licensure activities, and include them in a national plan?

5. Do small companies need advice on the licensing process?

6. Do manufacturing procedures and quality assurance tests need to be reviewed periodically? How can we assure they reflect the most up to date science?

BEST COPY AVAILABLE

Working Group #5

PRODUCTION AND PROCUREMENT

In the United States, the vaccine supplies are affected by a mix of public and private forces. Production is almost entirely in the hands of the private industry, but the Federal government now buys approximately half of the pediatric vaccine used in the country and the Army buys all the vaccine used by the military.

Even before the current concern about injury, liability and compensation, there was reluctance from industry to invest in new vaccines. Some firms left the vaccine business. In addition to the liability issue, experts have attributed the weak investment in vaccines to several factors: high R&D costs relative to potential sales; the relatively greater profit in drugs; the obvious limits to the sales volume, as a person does not receive a vaccine repeatedly; poor patent protection; the historically low price of materials used in public health programs; and uncertain international markets.

A careful review of the discussions about vaccine injury and liability has led to the conclusion that a Congressional remedy may be necessary to deal with immediate supply problems. Chairmen Dingell and Hatch ask that we look beyond the injury and liability issue as there has never been a specific commitment to producing new and improved vaccines for the long run. The charge to this working group is to identify what is necessary to ensure present and future vaccine availability. Keep in mind the vast increase in number of vaccines that can become available and the variety of technologies involved. Presumably this will require some strategic planning to increase production capacity so that new vaccines can be made available along with existing ones.

It is important that the working group consider existing production resources in the U.S. and abroad:

1. Will existing plants meet future national needs, particularly considering the range of new vaccines?

2. If not, what action is needed to ensure industry investment in plant or substitute government investment?

3. What changes or additions will be necessary to prepare plants to make many vaccines? How can planning for this be coordinated?

4. What are good ways of preserving existing vaccine production expertise and increasing capacity? How can supplies of vaccines be assured where the production level is small and not commercially attractive? If such a plant were maintained by the government would the industry give technical assistance? If so, on what basis?

BEST COPY AVAILABLE

5. At what point in time does a manufacturer need to know that supplies of a newly developing vaccine will be called for in order to prepare production facilities?

6. How early can target populations be identified by those who recommend use so that quantities of new vaccines can be predicted?

7. How can the government and industry best cooperate to meet national vaccine needs:

   - How can a system be developed that provides sufficient predictability on needed supplies to users and to manufacturers? How early can this be done in the planning for a new vaccine?
   - What is the optimal number of manufacturers per vaccine?
   - If there are several producers should government purchases be based on competitive pricing? Should market share be determined in advance? If so, on what basis?
   - Is supply assurance enhanced if manufacturers know their market share ahead of time, and if so, should the government commit to purchasing in bulk and reselling to practitioners? How should procurement policy be set?
   - If more than one licensed vaccine exists and one is more effective or safer but more costly, which should the government purchase? What criteria should guide such a decision?

8. To what extent and in what ways is the industry willing to participate in a national program?

   - Will it produce vaccines on a cost plus contract basis?
   - Are there other incentives and mechanisms which allow high priority vaccines to be produced at prices the nation and its consumers will pay?
   - What role might health insurers and employers play in a national program given the substantial savings inherent in disease prevention?

9. How can a national program contribute to the international commitment to immunize all of the world's children and other vaccine needs of developing countries?

10. Will there be increasing dependence on genetically engineered vaccines? How is the new science likely to affect production technology and resources?

11. What is the role for foreign producers in a national plan to implement public health priorities?

BEST COPY AVAILABLE

To state the problem in the most general way, a national plan would identify those vaccines of highest national priority for development, scale-up and production. Once the public health priorities have been established, there would need to be a reliable way to guarantee production. The working group should look at the possibilities, from continued reliance on the market system to government incentives to government procurement as used by the Army, to government production which is provided in statute as a last resort. Various combinations of these approaches might produce the most reliable supply.

BEST COPY AVAILABLE

Working Group #6

DISTRIBUTION AND USE

The Centers for Disease Control and the Advisory Committee on Immunization Practice currently produce recommendations on vaccine use. The Academy of Pediatrics has an independent process. Similarly, the Army and USAID have public processes for deciding who should receive which vaccines. State and local health departments help implement these recommendations. Although these efforts, including the Federally funded activities, have many of the characteristics of a national immunization program, there are serious flaws: inadequate funding; no control of research, development, and production; inadequate efforts on adult vaccines.

The task of this working group is to describe how to enhance the current efforts to optimize distribution and use of vaccines. Critical questions include:

1. At the start of a vaccine development project can the target population(s) be sufficiently well described to help industry make positive investment decisions? Can this be done at the point when the characteristics of the vaccine are known?

2. How should the nation pay for vaccines and their delivery? What part should be national policy? How can a national program make optimal use of local health departments, practitioners, and health care institutions? How can public education be enhanced?

3. How can an organized system of distribution and use best be linked to the program of production and procurement?

4. What special efforts are needed for adult vaccines?

5. How can more points of access to vaccine delivery be included in a national plan (i.e., health care institutions, work places, colleges, etc)?

6. How can efforts be improved to get pediatric vaccines to groups which don't receive them now although they are in great need (i.e., inner city poor, children on Indian reservations, some rural groups)?

7. How can use of pediatric vaccines at the early recommended times be improved rather than waiting until school entry? More use of day care centers? What else?

New strategies for immunization might emerge if the public health practitioners in the field had more involvement in the planning for vaccine research and development. Delivery systems could receive new emphasis. The recent success of immunization in the developing world is a tribute to attention to the problems of distribution and use.

BEST COPY AVAILABLE

Working Group #7

MONITORING AND SURVEILLANCE

To complete the elements of a national vaccine plan, the charge for this work group is to describe the elements of an effective program of monitoring and surveillance. Both disease monitoring, to understand the problems and goals of preventing vaccine preventable disease, and monitoring for effects and effectiveness of vaccines is needed. All elements of a national effort to use vaccines optimally are dependent on good data for assessment, quality control, and for future planning.

Important considerations include:

1. To what extent is the current monitoring and surveillance system sufficient to collect, analyze, and provide information to set priorities? What changes could improve a priority setting process?

2. Does the present system of data collection by CDC provide an adequate basis for disease comparisons? What is needed in addition?

3. Assessment of disease burden is essential to setting priorities for vaccine research, development, licensing, production and use. Who can do this descriptive epidemiology best?

4. How should the current quality control and oversight function of FDA relate to the surveillance and monitoring activities?

5. Can some of these activities be built into existing national surveys?

6. Which activities are most cost effective in terms of supporting a national vaccine program?

7. Can the cost of an adequate program be predicted?

8. Who should be responsible for designing each element of surveillance and monitoring systems? How much independence from operating agencies or companies is needed?

BEST COPY AVAILABLE

WORKSHOP ON VACCINE SUPPLY AND INNOVATION

Special Areas of Concern to the
Research Working Group

1. With respect to licensing, the same uniform criteria for adequate safety testing would be used regardless of the method of production of vaccine. It should be recognized that biotechnology has provided more precise means of producing vaccines and assuring their safety.

2. Within the last ten years the advent of biotechnology resulted in a virtual revolution in the capacity to produce new and better vaccines. This remarkable scientific development, which has potentially profound effects for the well being of the American public as well as that of the people of the developing world, has far outstripped the resources now available in this area. New resources, relatively small compared to those involved in the application of health and welfare measures, must encourage the continuum from basic research (the underpinning of all new vaccine development) through the discovery of new vaccines against specific infectious diseases and their clinical and field testing. In order to foster the vaccine research system it is necessary to ensure that when effective vaccines are developed in industry or academe their production, purchase and dissemination is endorsed. It is the sense of the group, therefore, that there be a considerable increase in the funding of the relevant research agency, NIAID, for basic research (where 28 vaccines are now in the advanced stages of development) for both laboratory and clinical research. The needs of industry should be considered through contract support, and purchase of effective vaccines. Additionally, increased funding should be provided for FDA to deal with the ever-increasing load of new vaccines for evaluation, and to CDC for the development of optimal means of delivery.

3. In order to realize our nation's enormous and increasing potential for the development, production and evaluation of novel or improved

BEST COPY AVAILABLE

vaccines, it is our opinion that an independent expert vaccine advisory group should be created which would include representatives from interested governmental agencies (NIH, FDA, CDC, and DOD), industrial concerns, academia and non-governmental funding organizations. The purpose of this advisory group would be the facilitation of effective communication to encourage vaccine development and the insurance of adequate funding for this pursuit. We recommend that this advisory committee be established and report to an office within the government chosen to maximize its impact and ability to achieve these stated goals.

BEST COPY AVAILABLE

ROBERT T. STAFFORD, VERMONT
EDWARD M. KENNEDY, MASSACHUSETTS
PAULA HAWKINS, FLORIDA
STROM THURMOND, SOUTH CAROLINA
LOWELL P. WEICKER, JR., CONNECTICUT
ORRIN G. HATCH, UTAH
CHRISTOPHER J. DODD, CONNECTICUT
PAUL SIMON, ILLINOIS
JOHN F. KERRY, MASSACHUSETTS
RONALD F. ROCKEN, STAFF DIRECTOR
KATHRYN ST. MEDARD, MINORITY STAFF DIRECTOR

United States Senate

COMMITTEE ON LABOR AND
HUMAN RESOURCES
WASHINGTON, DC 20510

May 19, 1986

Dr. Samuel Thier
President - Institute of Medicine
National Academy of Sciences
2101 Constitution Avenue, N. W.
Washington, D. C. 20418

Dear Dr. Thier:

I am writing to express my appreciation to the Institute of Medicine for putting together the workshop on vaccine innovation and supply on April 24 and 25, 1986. I'm told by my staff that you assembled quite a group of experts! The discussion was reportedly productive, and many useful ideas were generated.

Hopefully, the Congress and Administration, spurred on by your deliberations, can work together to improve the current system of vaccine development, production and usage.

Sincerely,

Orrin G. Hatch
Chairman

OGH:chb

BEST COPY AVAILABLE